NEUROIMAGE **5,** 261–270 (1997)
ARTICLE NO. NI970269

Cognitive Conjunction: A New Approach to Brain Activation Experiments

C. J. Price and K. J. Friston

The Wellcome Department of Cognitive Neurology, Institute of Neurology, Queen Square, London WC1N 3BG, United Kingdom

Received October 3, 1996

This paper introduces the concepts and procedures of "cognitive conjunction," a new approach to designing and analyzing cognitive activation experiments. Cognitive conjunction compliments categorical approaches such as cognitive subtraction and requires a specific form of statistical inference that involves the conjunction of several hypotheses. While cognitive subtraction studies are designed such that a pair of tasks differ only by the processing component(s) of interest, cognitive conjunction studies are designed such that two or more distinct task pairs each share a common processing difference. The neural correlates of the process of interest are then associated with the common areas of activation for each task pair. There are two main advantages of cognitive conjunction relative to cognitive subtraction. The first is that it provides a greater latitude for selecting baseline tasks because it is not necessary to control for all but the component of interest. The only constraint on selecting the baseline is that the component of interest is the only process that differs in each task pair. The second advantage is that cognitive conjunction does not depend on "pure insertion"—the assumption that the addition of an extra processing component in the activation task has no effect on the implementation of processes that are also engaged by the baseline task. The differences between the design and the statistical analysis of experiments based on cognitive subtraction, cognitive conjunction, and factorial designs are illustrated with a study of phonological retrieval. Cognitive conjunction analysis indicates that irrespective of whether subjects name words, objects, letters, or colors, there is activation of the left posterior basal temporal lobe, the left frontal operculum, the left thalamus, and the midline cerebellum. © 1997 Academic Press

INTRODUCTION

Cognitive subtraction has been the mainstay of experimental design since the inception of cognitive activation studies in the late eighties. Subtraction designs involve selecting an activation task that engages the cognitive component of interest and a baseline task that activates all but the component of interest. The experimental design can be elaborated further by the addition or deletion of separable cognitive components to the tasks. Brain regions associated with the added cognitive components are identified by serial subtraction of scans obtained during the different tasks, by assuming that (i) the extra activations are due to the added cognitive component and (ii) the brain's implementation of previous components remains unchanged.

One of the problems with designing cognitive subtraction studies is finding baseline tasks that activate all but the process of interest. For instance, even when a baseline task does not require the explicit involvement of a cognitive process, there can be implicit processing, beyond the demands of the task, that reduces the difference between the activation and the baseline tasks (Price *et al.,* 1996). Another problem with cognitive subtraction is the effect that added components have on previous components. In general, for cognitive subtraction to work, we have to assume that the interaction between new and existing components can be ignored. This assumption is known as *pure insertion,* wherein a new cognitive component can be purely inserted without affecting the expression of previous ones (i.e., those shared by both activation and baseline tasks). More generally, however, the expression of shared components is affected when new components are added and the difference between two tasks will comprise the added task component and the interaction between the added and the shared components (see Friston *et al.,* 1996 for further discussion).

The approach presented in this paper addresses and attempts to resolve both of these issues by introducing the idea of cognitive conjunctions. Cognitive conjunctions are an extension to the cognitive subtraction paradigm. While cognitive subtraction looks for activation differences between a pair of tasks, cognitive conjunction looks for the commonality in activation differences (i.e., subtractions) between two or more pairs of tasks that share only the component of interest. Figures 1a and 1b illustrate this difference.

Figure 1a represents a cognitive subtraction hierar-

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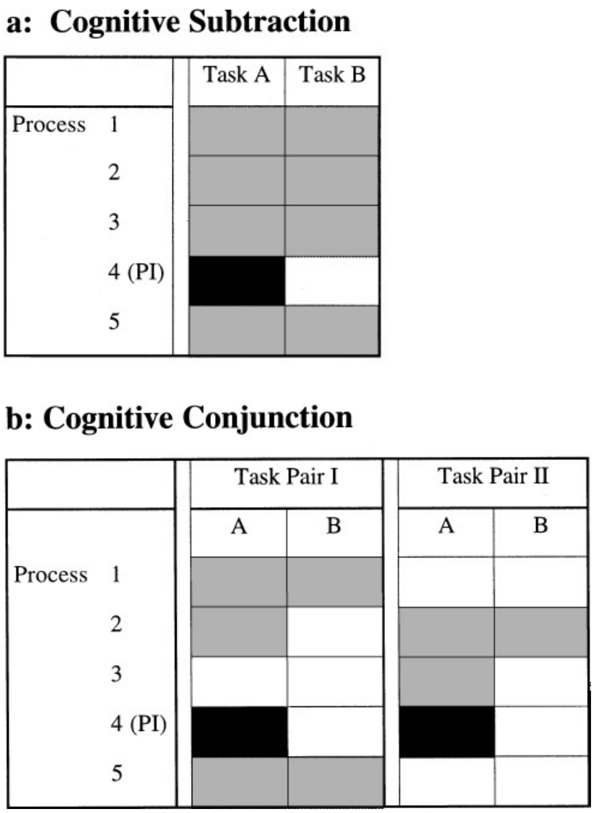


FIG. 1. (a) A cognitive subtraction hierarchy. PI is the process of interest, A is the activation task, and B is the baseline task. (b) A cognitive conjunction design which has two task pairs (I and II) each with an activation (A) and baseline (B) task. P1, P2, P3, and P4 are distinct but arbitrary task components.

chy. The process of interest (PI) is revealed by subtracting activity during the baseline task (B) from that during the activation task (A). Figure 1b represents a cognitive conjunction design which has two task pairs (IA, IB and IIA, IIB) designed such that the cognitive differences between the tasks of each pair both contain the PI. Regional activation associated with PI is revealed by finding areas activated in both independent subtractions (IA − IB and IIA − IIB). For IA − IB, the differences are {P2, P4} and for IIA − IIB the differences are {P3, P4}. P4 (= PI) is activated in both comparisons; P2 and P3 are distinct but arbitrary task components.

This paper is divided into two sections. The first section introduces and discusses the concept of cognitive conjunction. The second section describes the procedures of analysis using a PET study of stimulus naming to identify the brain regions that implement phonological retrieval. We will show that conjunction analysis (i) allows the identification of the functional anatomy of cognitive processes, without relying on pure insertion, and (ii) provides a greater latitude for task selection by removing the constraints on the choice of baseline task imposed by cognitive subtraction.

COGNITIVE CONJUNCTION

Task Selection

Cognitive conjunction uses a series of activation and baseline task pairs to define a set of differences. These differences can include many cognitive components but only the component of interest is common to all task pairs. The activation conjunction is identified by the conjoint testing of several hypotheses, each pertaining to individual subtractions or effects. By identifying the areas of common activation we can associate these regional effects with the common processing component. The only restriction on the baseline tasks is that differences between task pairs both contain the PI. They do not have to control for all the noninteresting components of the activation task. This allows for a flexible and less constrained choice of baseline tasks: The baseline tasks could be the same for all pairs (e.g., an independent rest scan for each pair) or specific to each pair, sharing a greater or lesser number of processes with the activation tasks. In other words they could be very similar or very different depending on the experimental question. For example, baseline tasks could differ substantially from activation tasks that involve some explicit processing, so as to avoid implicit processing in the former.

Interactions and "Pure Insertion"

Cognitive conjunction differs fundamentally from cognitive subtraction at both the level of experimental design and the analysis. One design difference is that cognitive conjunction is not serial (where each successive task serves as a baseline for the next); like factorial designs each activation task has its own baseline, such that each subtraction is independent of the other subtractions included in the conjunction. Another difference, mentioned above, is that the baseline and activation tasks are not constrained to differ by a single cognitive component. An important point here is that cognitive components that are not common to all task pairs can include interaction terms (i.e., the interaction between an added component and the shared components). Because these effects are discounted in the conjunction analysis, one does not need to rely on pure insertion. The reason that cognitive conjunctions do not rely on pure insertion is that the conjunction discounts interaction terms whether they exist or not. In other words a conjunction of activations only qualifies as such, if these activations are not rendered significantly different by interaction effects (this of course assumes that different interactions do not activate the same area to the same degree). Cognitive subtraction on the other hand assumes these interaction terms *do not exist*. This can be seen clearly in Fig. 1b. Above we had assumed that P2 in the first task pair and P3 in the second task pair were distinct and novel cognitive processes. However, they could also be construed as interaction effects; i.e., P2 could represent the interaction between P1 and PI and in the second task pair P3 could represent the interaction between P2 and PI. By virtue of the fact that the conjunction involves PI, and only PI, the interaction effects are discounted even if they are substantial.

Another way of looking at interactions is to regard them as "context-sensitive" activations, in other words activation effects that are seen only in a particular context (the context with which the process of interest is interacting). In this sense conjunction analyses can be thought of as testing for the activating effect of a particular process in a whole series of contexts (i.e., series of task pairs). By retaining areas that activate equally in all "contexts" we can identify robust, "context-insensitive" activations that can be attributed to the process per se, and not some interactional effect.

Statistical Considerations

At the level of statistical analysis there are differences between the way one tests for subtractions and conjunctions. In cognitive subtraction, an area of activation is identified by subtracting one task from another; in other words testing for a single effect. Conjunction analyses, on the other hand, rely upon the conjoint testing for multiple effects (e.g., a significant activation in the first and the second task pairs). We expand briefly on this distinction below and more formally in the Appendix.

Functional neuroimaging studies are usually analyzed using some form of statistical parametric mapping (SPM). This involves the construction of statistical images that test hypotheses about differences in the distribution of brain activity among tasks. There are many ways that one could test for conjunctions; we have chosen a particular approach that is implemented easily in the context of SPM. In this approach, we essentially create an SPM of the sum of all the activations and eliminate voxels where differences among these effects are significant. The rationale for this can be seen in relation to factorial designs. For example, consider two task pairs, whose activations can be thought of as reflecting the presence of a common cognitive component in two contexts or under two levels (i.e., the level of the first task pair and level of the second task pair). These activations can be thought of as two *simple main effects.* A conjunction is defined as the presence of a *main effect* in the absence of an *interaction*. In other words, the activation or main effect is significant and the simple effects are not significantly different. Using this definition of a conjunction, we distinguish between main effects with and without interactions. The latter do not constitute conjunctions and normally the two simple effects should be reported separately. By virtue of this, a conjunction analysis can be used to complement the usual analysis of factorial designs. In summary the main effect is the conjoint expression of the series of simple effects (i.e., activations) one is testing for. A conjunction is defined as a significant main effect in the absence of any differences or *interactions* among the simple effects. The conventional statistical wisdom is that it does not usually make sense, either statistically or scientifically, to test for main effects in the presence of an interaction (Nelder, 1977). A conjunction therefore resolves this problem by discounting main effects when there is evidence for an interaction. The mathematical details of the conjunction analysis are presented in the Appendix for the interested reader.

A PET STUDY OF NAMING

This section describes the cognitive model, experimental design, and functional analysis (i.e., how each task decomposes into separable components) of a PET study which uses a cognitive conjunction design to identify the brain regions involved in phonological retrieval. We ascribe the term phonological retrieval to the activation of the verbal label (i.e., the name) attached to a visual stimulus or concept. The stimuli chosen for the study were words, letters, objects, and colors.

Cognitive Model

Figure 2 is the cognitive model on which we have based our experimental design; it specifies the processing components involved in each naming task and

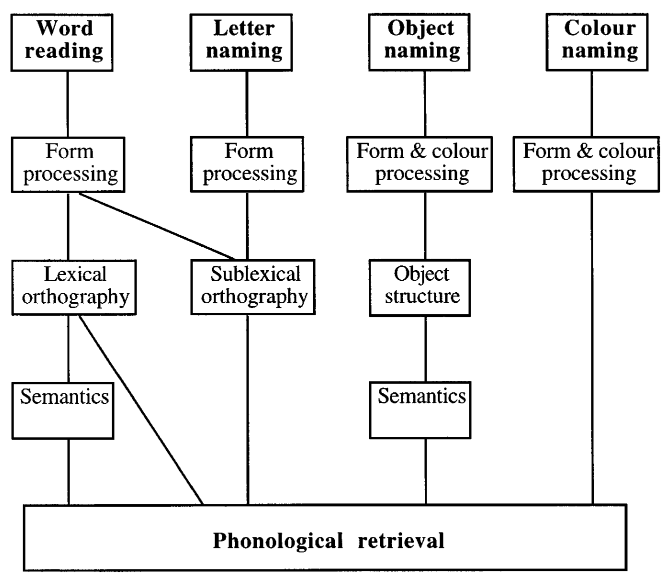


FIG. 2. A cognitive model of the processing components involved in reading, letter naming, object naming, and color naming.

emphasizes the convergence of different routes to phonological retrieval.

For each perceptual category (i.e., words, letters, objects, or colors) there will be a specific set of processes required to retrieve the name. For instance, during object naming phonological retrieval is dependent on the activation of both structural and semantic memories; during reading, phonological retrieval can proceed via sublexical pathways (for instance, when we read pseudowords like "neeb" that have no semantic content), and during color naming, phonological retrieval is not dependent on either structural or semantic memories. The aim of the cognitive conjunction is to identify activation that is common to naming each perceptual category irrespective of the processing route taken. From a cognitive perspective, the conjunction of these tasks includes the retrieval and execution of phonology.

Experimental Design

Four pairs of activation (A) and baseline (B) tasks were used to identify the brain regions implicated in phonological retrieval. Illustrations of the stimuli are shown in Fig. 3.

Below we list the constituent cognitive components of the activation and baseline tasks and the differences for each task pair. It will be seen that phonological retrieval is the only cognitive component common to all task pair differences.

Task Pair I: Word Naming

This task pair comprised (A) reading single familiar monosyllabic words (task 1) and (B) saying the same prespecified word to strings of false font (task 2). The cognitive components common to both these tasks were early visual analysis and articulation. The differences between these two tasks includes orthographic, semantic, and sublexical processing; phonological retrieval; and the interactions among these components.

Task Pair II: Letter Naming

This task pair comprised (A) naming single arabic letters (task 3) and (B) saying the same prespecified word to single false-font characters (task 4). The cognitive components common to both these tasks were early visual analysis and articulation. The differences between these two tasks include orthographic letter processing, phonological retrieval, and the interaction between these processes.

Task Pair III: Object Naming

This task pair comprised (A) naming visually presented easily identifiable objects (task 5) and (B) saying "yes" to the same stimuli (task 6). The cognitive components common to both these tasks were early visual

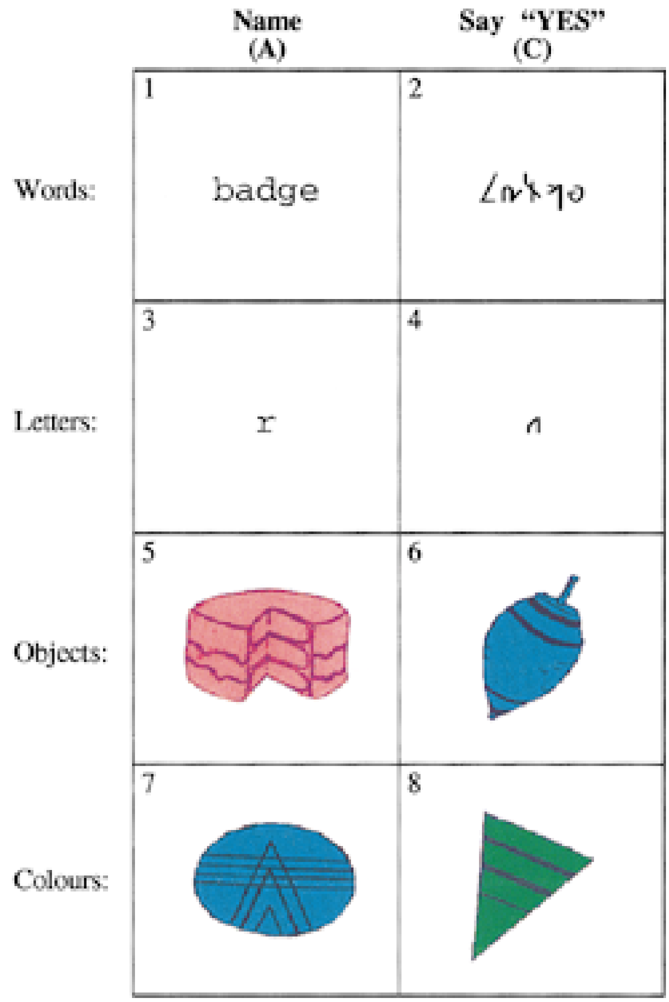


FIG. 3. Illustrations of the stimuli used in the experiment.

analysis, object processing (3D form processing and activation of structural and semantic memories), and articulation. The differences between these two tasks include explicit phonological retrieval and the interaction between object recognition and phonological retrieval.

Task Pair IV: Color Naming

This task pair comprised (A) naming the color of 2D patterns (task 7) and (B) saying "yes" to the same stimuli to acknowledge the stimulus had been seen (task 8). The cognitive components common to both these tasks were early visual analysis of form and color and articulation. The differences between these two tasks include phonological retrieval and the interaction between visual analysis and phonological retrieval.

Functional Analysis of Tasks

Figure 4 represents a graphic task analysis where we have represented each of the four task pairs in terms of

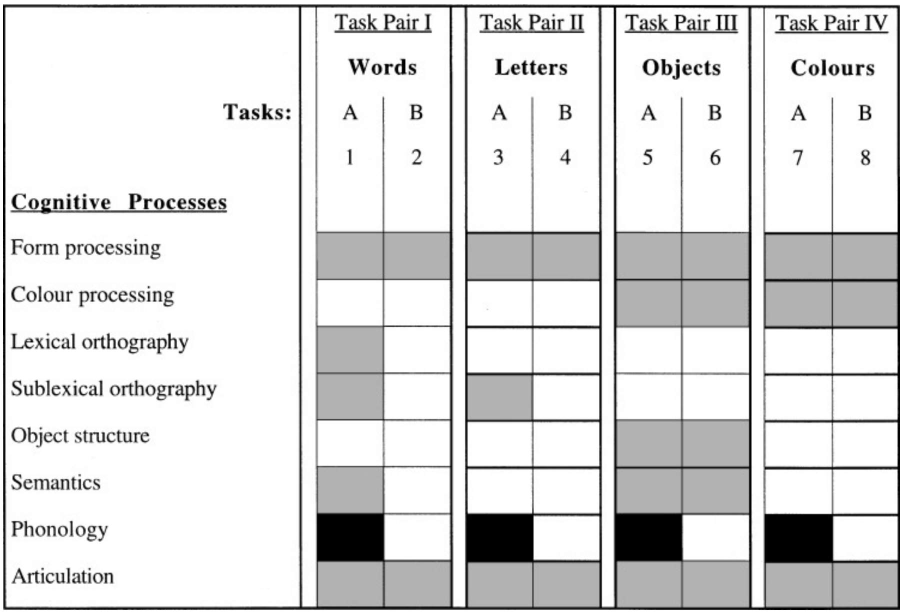


FIG. 4. A graphic task analysis of the constituent processing components of the experimental conditions. The format corresponds to that adopted in Fig. 1 but the constituent processing components used are those illustrated in the cognitive model of Fig. 2. The gray-filled regions indicate task components that distinguish between activation and baseline tasks; the black-filled regions indicate where these differences were common for every pair.

their constituent processing components. The format corresponds to that adopted in Fig. 1 but the constituent processing components used are those illustrated in the cognitive model of Fig. 2. The gray-filled regions indicate task components that distinguish between activation and baseline tasks; the black-filled regions indicate those differences common to every pair. It is immediately apparent that the only cognitive component that distinguishes between all task pairs is phonological retrieval.

Data Acquisition and Analysis

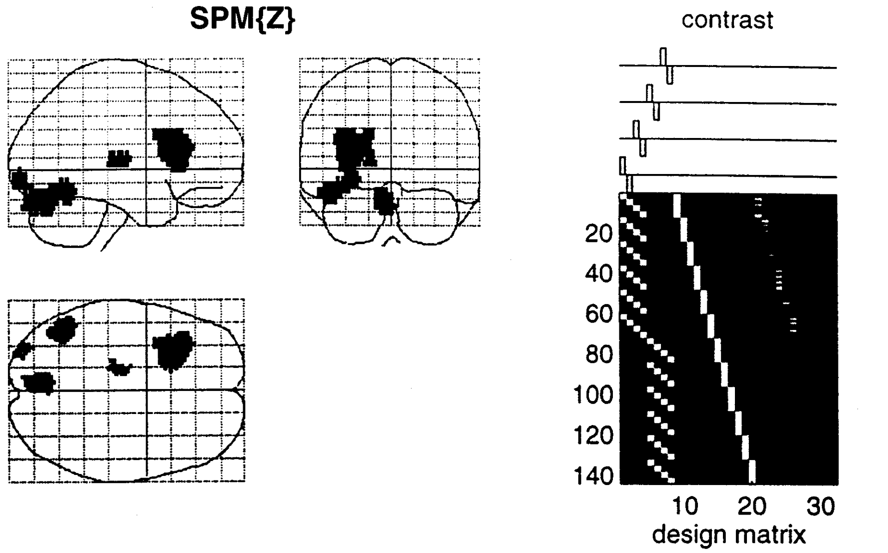
Each task pair was replicated three times in one of two groups of six subjects. One group named words and letters with the respective baselines, the other named pictures and colors. The data were acquired using PET and a bolus $H_2{}^{15}O$ technique as previously described, realigned, spatially normalized (Friston *et al.*, 1996), and analyzed with statistical parametric mapping using ANCOVA with global activity as a subject-specific confounding covariate. Four orthogonal contrasts were specified, each testing for activations within each of the four task pairs, which were used in the conjunction analysis as described in the Appendix.

RESULTS

The SPM illustrating the maximum intensity projection of the Z statistic for the conjunction of the task pair differences is shown in Fig. 5. It can be seen that three regions surviving a corrected ($P < 0.05$) threshold were identified; the left posterior basal temporal lobe (Brodmann's area 37), the left frontal operculum (from the left anterior insula to the lateral inferior prefrontal cortex), and the midline cerebellum. There were also conjoint activations, which only reached an uncorrected threshold of significance, in the left thalamus and the left lateral inferior occipital lobe. Figure 6 plots the adjusted mean activity for all eight conditions in these regions to illustrate the activation differences for all four independent task pairs.

DISCUSSION

In this paper we have introduced the idea of ascribing a function to a particular brain region on the basis of conjoint activations by pairs of tasks that each share a common processing difference. This can be thought of as an extension of categorical analyses in the sense that we combine many independent subtractions in order to identify a conjunction of activations. For conjunctions to be implemented, the activation task in each pair must (i) engage the process of interest and (ii) have its own baseline. These design prerequisites contrast to those of subtraction designs (where each successive task serves as a baseline for the next) but resemble factorial designs. Below we reiterate and expand upon the differences between cognitive subtraction, factorial designs, and cognitive conjunctions.



Regions of significant conjunction

set-level {c}		cluster-level {k,Z}		voxel-level {Z}		uncorrected k & Z		x,y,z {mm}		
0.001	**(5)**	**0.001**	**(524, 4.96)**	**0.004**	**(4.96)**	**0.000**	**0.000**	**−26**	**20**	**12**
				0.006	(4.89)		0.000	−34	26	16
				0.079	(4.27)		0.000	−20	18	20
		0.024	**(174, 4.66)**	**0.016**	**(4.66)**	**0.008**	**0.000**	**−44**	**−62**	**−16**
				0.050	(4.38)		0.000	−48	−56	−20
				0.871	(3.27)		0.001	−42	−72	−16
		0.037	**(169, 4.39)**	**0.049**	**(4.39)**	**0.008**	**0.000**	**−8**	**−78**	**−20**
				0.761	(3.40)		0.000	0	−74	−32
		0.293	**(51, 3.89)**	**0.273**	**(3.89)**	**0.116**	**0.000**	**−32**	**−92**	**−8**
		0.353	**(34, 3.81)**	**0.334**	**(3.81)**	**0.194**	**0.000**	**−12**	**−18**	**4**
				0.553	(3.60)		0.000	−18	−24	8

Height threshold {u} = 3.09, p = 0.001
Extent threshold {k} = 30 voxels, p = 0.221
Expected voxels per cluster, E{n} = 21.5
Expected number of clusters, E{m} = 0.7

Volume {S} = 69850 voxels or 344.6 Resels
Degrees of freedom due to error = 114.0
Smoothness {FWHM mm} = 13.9 15.2 15.3
{voxels} = 5.9 6.5 6.5

FIG. 5. The SPM illustrating the maximum intensity projection of the Z statistic for the conjunction of the four task pair differences.

Cognitive Subtraction

The simplest form of subtractive design involves a task that activates the cognitive process of interest and a second task that controls for all but the process of interest. Subtraction designs can also be elaborated into serial or hierarchical subtraction when the baseline task involves one more cognitive component than a third task. A good example of a hierarchical subtractive design is the study of reading by Petersen *et al.* (1990). This study had one variable with five different levels relating to the type of visual stimuli viewed: words, pseudowords, consonant letter strings, false font, and visual fixation. A cognitive subtraction analysis identifies differences in activation between different levels of the hierarchy and associates these with the differences in psychological processes between levels. As discussed above, there are two main limitations of cognitive subtraction studies. The first is that they rely on pure insertion which assumes that an extra cognitive component can be purely inserted without affecting the expression of preexisting components. The second relates to the difficulty of finding baseline tasks that activate all but the process of interest. This is particularly relevant when there is implicit processing of a stimulus beyond the demands of a task (see Price *et al.*, 1996).

Factorial Designs

In factorial designs, there are two or more variables (or factors) and the different levels of each variable are

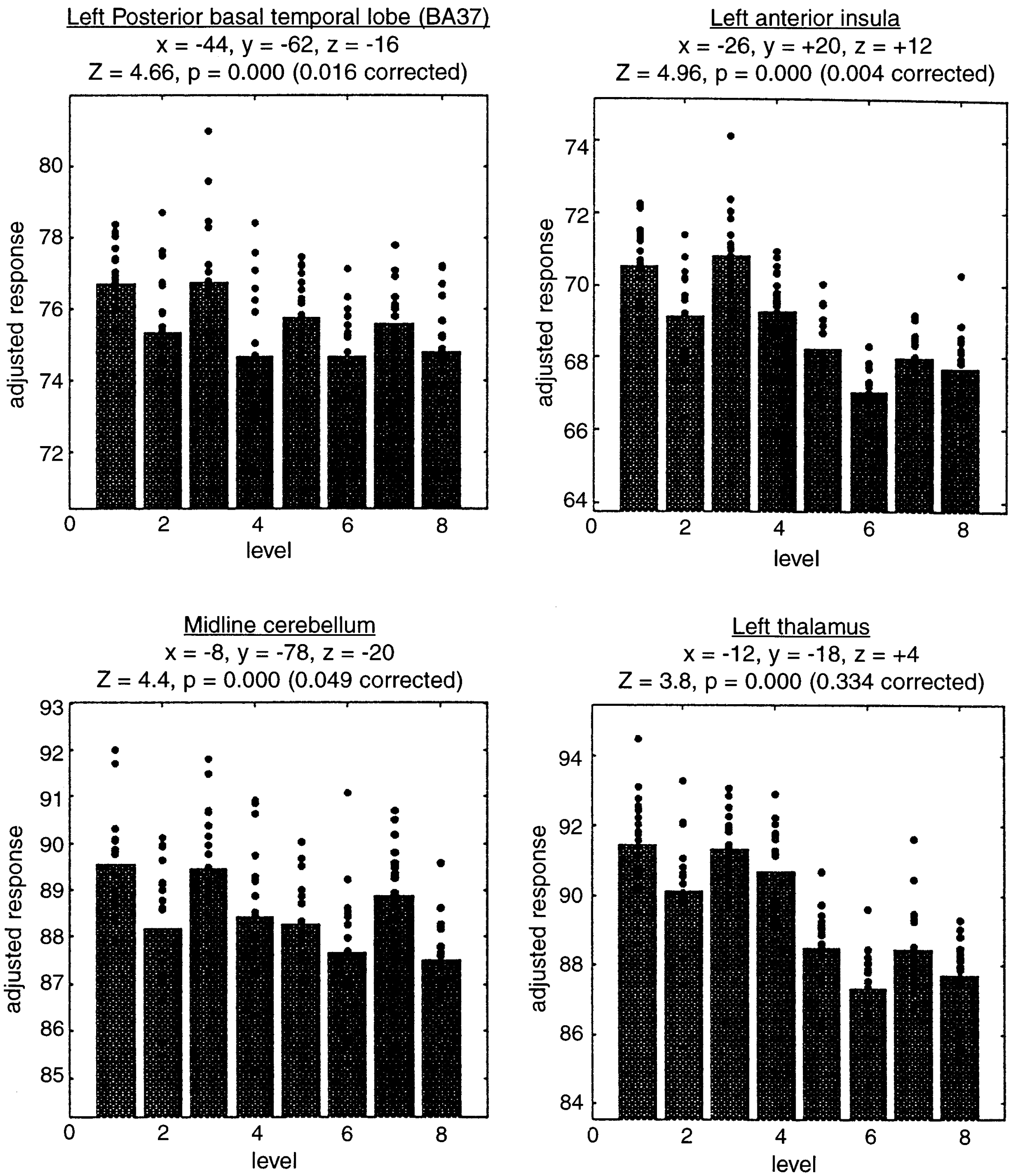


FIG. 6. The adjusted mean activity for all eight conditions in the regions identified by the conjunction analysis.

matched. For example, if the two variables were phonological retrieval and object recognition, the simplest factorial design would have four tasks which evaluated (i) phonological retrieval in the presence of object recognition, (ii) phonological retrieval in the absence of object recognition, (iii) object recognition in the absence of phonological retrieval, and (iv) neither object recognition nor phonological retrieval. This design would allow the effect that one variable has on the expression of the other variable to be measured explicitly. By convention, the analysis of factorial designs involves calculating the main effects of each variable and the interaction between them. The main effects in activation studies identify the brain areas where there is more activation in the sum of the activation tasks than in the sum of the baseline tasks (e.g., tasks with phonological retrieval − tasks without phonological retrieval and tasks with object recognition − tasks without object recognition).

The interaction between variables identifies areas where the effect of one variable varies depending on the presence or absence of another variable.

Factorial designs have several important advantages over simple subtraction designs. First, they allow greater generalizability of the results because the level effects can be specified for each factor (as in pure subtraction) or generalized for all factors. Second, and most important, when the effect of one factor level varies according to the level of another factor, factorial designs allow us to verify the significance of this difference with the interaction term (see Friston *et al.*, 1996). A main effect can be observed with or without an interaction. If there is an interaction the interpretation of the main effect becomes more complicated and usually calls for an analysis of the simple main effects (i.e., the effects of one factor under a single level of the other). It is therefore important to distinguish between main effects in the presence and absence of an interaction. A conjunction analysis can be used to do this.

Cognitive Conjunctions

In terms of analysis, the main effect in a factorial design includes the sum of task pair differences irrespective of whether there is differential activation between task pairs (i.e., an interaction). A conjunction analysis departs from this convention by identifying areas where there is a significant main effect in the absence of an interaction. In other words, areas are identified in which task-pair effects are jointly significant and are not significantly different. Although cognitive conjunction designs resemble those of factorial designs insofar as each activation task has its own baseline, there can also be distinct differences in the design and analysis of these approaches. When the experimental design is factorial, there are two or more factors or variables and the different levels of each variable must be matched across task pairs (see above). In contrast, the different levels of each task do not need to be matched in cognitive conjunction designs and the activation and baseline tasks are not constrained to differ by a single cognitive component. The baselines could, theoretically, all involve the same task (e.g., a rest condition for each activation condition), providing that the difference between any two tasks, in cognitive terms, includes the component of interest.

By excluding areas that differentially activate, even though they may be significantly activated in each task pair, the analysis of cognitive conjunctions is more conservative or restrictive than that of cognitive subtractions and factorial designs. The conservative nature of cognitive conjunction, however, enables us to distinguish areas that are functionally specialized from areas that are not. For instance, if the activation of an area by phonological retrieval depended upon the presence of color (i.e., there was a significant interaction between color naming and another naming task), this would imply that the area was specialized for the integration of phonological retrieval and color processing rather than being dedicated to phonological retrieval per se. On the other hand if an area responds to, and only to, phonological retrieval (i.e., it is unaffected by the type of naming task or the context in which names were generated), then a true conjunction will ensue, implying that the area is specialized for phonological retrieval irrespective of other processing requirements. In summary, the conjunction of activations that are not significantly different defines functionally specialized areas, whereas simply demonstrating common activations (in the main effect) implies specialization but only in relation to some other processes or systems. On the basis of this argument, it can be seen that a conjunction analysis identifies a very specific sort of functional attribution that can be powerfully complimented by an analysis of interaction effects (see Friston *et al.*, 1996).

Another important aspect of cognitive conjunctions is that, like factorial designs, they do not depend on "pure insertion." In general, the difference between an activation and a baseline task pair involves not only the extra cognitive component but also the interaction of this added component with processes shared with the baseline task. Cognitive subtraction assumes these interactions do not exist, factorial designs measure the interaction effects explicitly, and cognitive conjunctions discount regions that express them (because the interactions are unique to each task pair or can be made so by experimental design).

Functional Specialization for Naming

The experiment we have used to illustrate the design and analysis of cognitive conjunction studies investigated the brain regions activated when subjects retrieve the phonology of visually presented stimuli. The activation tasks involved naming words, letters, objects, and colors, and each of these tasks had a corresponding baseline that did not involve explicit naming. The processing differences between task pairs varied but the one consistent difference was explicit phonological retrieval. The conjunction of activations for each task pair was identified by the conjoint testing of several hypotheses. Areas activated equally by each task pair were the left posterior basal temporal lobe (Brodmann's area 37), the left frontal operculum, and the midline cerebellum. Lesion studies have shown that damage to any of these areas impairs naming (Mesulam, 1990). Using a cognitive conjunction study, we have demonstrated that these areas are functionally segregated for phonological retrieval from visually presented stimuli.

Previous studies that have used cognitive subtraction to identify areas involved in phonological retrieval have been hindered by the difficulty of finding task pairs that differ only in terms of phonological retrieval. For instance, any task that presents word-like stimuli to control for orthographic and semantic processing also activates phonological processes implicitly. Using a cognitive conjunction approach, orthographic and semantic processing do not have to be controlled in the word task pair because the areas associated with phonological retrieval are identified by finding the processing areas that are shared by reading and other naming tasks.

CONCLUSION

In this paper we have presented a simple variant on experimental design and analysis of functional imaging data that facilitates the identification of brain systems implementing specific cognitive components. This approach is based upon, but less constrained than, cognitive subtraction and should provide for a greater latitude of experimental design and possible retrospective analysis of previously reported studies. We hope that this reasonably simple embellishment of existing experimental and analysis strategies will further refine our understanding of functional specialization and segregation in the brain.

APPENDIX

In this Appendix we present the details of how we construct SPMs to test for the conjunction of two or more hypotheses. Although there are a number of ways in which one could test for the conjoint expression of two or more effects, we have the special problem of formulating such a test so that can be used in the context of statistical parametric mapping (and implicitly the theory of Gaussian fields). In brief the solution we have adopted consists of creating a SPM that reflects the sum of all the effects one is interested in and then eliminating regions where there are significant differences among these effects. In this approach a conjunction corresponds to a significant sum of all the effects if, and only if, there are no significant differences among them. This second condition confers the essence of a conjunction: For example; consider two effects evidenced by high values of some statistic, say z_1 and z_2. The sum of these numbers would be an appropriate statistic for the assessment of the first *or* second hypothesis because either a large z_1 or a large z_2 can give a high value of $z_1 + z_2$. However, a conjunction requires the first *and* second hypotheses to be true. This is the case if z_1 and z_2 are high and are not significantly different. For readers familiar with factorial designs this can be construed as identifying main effects in the absence of an interaction. It should be noted that conjunctions discount activations that are significantly different even if they are all significant in their own right.

A more general formulation of conjunctions can be framed in terms of main effects and interactions. In this formulation the *main effect* is the conjoint expression of the series of simple effects one is testing for. A conjunction is defined as a significant main effect in the absence of any differences or *interactions* among the simple effects. The conventional wisdom is that it does not usually make sense, either statistically or scientifically, to test for main effects in the presence of an interaction (Nelder, 1977). A conjunction therefore resolves this problem by discounting main effects when there is evidence for an interaction.

An issue that is specific to SPMs is that we want to eliminate voxels that show an interaction in a way that is independent of identifying voxels that show a conjoint or main effect. This is important because the elimination of regions, where significant differences are observed, can be used to reduce the search volume, rendering the correction for multiple comparisons less severe and the analysis more sensitive.

In what follows we present the details of the approach for the general problem of testing for the conjunction of N effects in the context of the linear model,

$$\mathbf{y} = \mathbf{X} \cdot \boldsymbol{\beta} + \mathbf{r},$$

where $\mathbf{y}$ is the response variable (e.g., rCBF), a column vector with one element for each scan. $\mathbf{X}$ is the design matrix modeling the effects, with one effect in each column and one row for each scan. The parameter column vector $\boldsymbol{\beta}$ contains one element for each effect in $\mathbf{X}$. $\mathbf{r}$ is a column vector of identically and independently distributed Gaussian residuals.

The problem can be formulated as follows: The N hypotheses can be specified in terms of a set of contrasts (e.g., a matrix $\mathbf{C}$ with one contrast per column, i.e., $\mathbf{C} = [\mathbf{c}_1, \mathbf{c}_2, \ldots, \mathbf{c}_N]$) that specify linear compounds of parameter estimates (e.g., task condition means) where the compounds (e.g., activations) are weighted by the elements in the column vectors $\mathbf{c}_1, \mathbf{c}_2, \ldots$. We now wish to construct a SPM that reflects the conjoint expression of the effects specified by $\mathbf{c}_1, \mathbf{c}_2, \ldots$ and to eliminate regions where there are differences or interactions among these effects. First we note, from linear models theory, that the improvement in sums of squares in a nested sequence of models is independent, even in the nonnull case. In particular, suppose we fit the sequence of models,

$$M_0: \quad \mathbf{y} = [\mathbf{X}_r] \cdot \boldsymbol{\beta}_0 + \mathbf{r}_0,$$

$$M_1: \quad \mathbf{y} = [\mathbf{X}_i\ \mathbf{X}_r] \cdot \boldsymbol{\beta}_1 + \mathbf{r}_1,$$

$$M_2: \quad \mathbf{y} = [\mathbf{X}_c\ \mathbf{X}_i\ \mathbf{X}_r] \cdot \boldsymbol{\beta}_2 + \mathbf{r}_2,$$

where the $\mathbf{X}_c$, $\mathbf{X}_i$, and $\mathbf{X}_r$ represent mutually orthogonal partitions of the original design matrix $\mathbf{X}$. These partitions embody the conjunction of simple effects specified in $\mathbf{C}$, the differences or interactions among these effects and all remaining effects, respectively. $\mathbf{X}_r$ is $\mathbf{X}$ orthogonalized with respect to $\mathbf{X}_s$, where $\mathbf{X}_s$ is the space spanned by the simple effects of interest; $\mathbf{X}_s = \mathbf{X} \cdot \mathbf{C}$. $\mathbf{X}_i$ is $\mathbf{X}_s$, orthogonalized with respect to $\mathbf{X}_c$ and $\mathbf{X}_c$ is the main effect of interest $\Sigma\mathbf{X} \cdot \mathbf{c}_i$. We can now test for interactions by comparing M_0 with M_1 and for the main effect of interest by comparing M_2 with M_1, in such a way that these tests are based on independent statistics (under the null hypothesis).

Let R_0, R_1, and R_2 denote the error sums of squares and the degrees of freedom be d_0, d_1, and d_2 for the three models. Then $(R_0 - R_1)$, $(R_1 - R_2)$, and R_2 are all independent (noncentral) χ^2 random variables with degrees of freedom $(d_0 - d_1)$, $(d_1 - d_2) = 1$, and d_2, respectively. From this it follows that the sequential F statistics,

$$F_i = \frac{(R_0 - R_1)/(d_0 - d_1)}{R_1/d_1}, \quad F_c = \frac{(R_1 - R_2)/(d_1 - d_2)}{R_2/d_2},$$

are independent provided $(R_1 - R_2)$ and R_2 are central, i.e., there is truly no main effect. This is the case under the null hypothesis, which we are trying to protect against. This means that we can eliminate voxels that show an interaction using F_i and then use F_c to construct the SPM testing for the main effect to give us the conjunctions. The advantage of this formulation is that F_c has *exactly* a $F_{1,d2}$ distribution, irrespective of the presence of interactions. The distribution of F_i when there is a main effect, is not a (central) F distribution because the denominator now contains sums of squares due to this main effect. However, this does not invalidate the procedure; the elimination step is not a hypothesis test, so there is no false-positive rate to control.

The resulting SPM$\{F\}$ can also be represented as an SPM$\{t\}$ [or, after transformation, SPM$\{Z\}$]. This is because F_c is the corresponding t value squared. The SPM$\{F\}$ will show conjoint activations and deactivations, whereas the SPM$\{t\}$ will only show one tail (i.e., common activations). Both the SPM$\{F\}$ and the SPM$\{t\}$ can now be subject to standard inferential procedures based on the theory of Gaussian random fields (Worsley, 1994; Friston *et al.*, 1994).

Extension for Serially Correlated fMRI Data

The analysis above depends on the assumption that the error terms are independent. In some instances this may not be the case: In functional magnetic resonance imaging with short repetition times, and temporal smoothing, there may be serial correlations between successive observations that can be modeled by an autocovariance matrix Σ. In this instance F_i and F_c can be obtained as the ratio of the appropriate sums of squares divided by their expectation, given by trace $(\mathbf{R} \cdot \Sigma)$. $\mathbf{R}$ is the residual (or difference in residual) forming matrix corresponding to the sum of squares in question. The resulting statistics are then approximately distributed according to the F distribution, where the *effective* degrees of freedom of this distribution are as described in Worsley and Friston (1995).

ACKNOWLEDGMENTS

This work was funded by the Wellcome Trust. We thank our colleagues for invaluable discussion, especially Richard Frackowiak. We thank the reviewers for substantial help, particularly reviewer 2 who suggested the sequential F ratio approach adopted in this work. We also thank Caroline Moore for her help acquiring the data and John Herries for his help with the figures.

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